201-14672

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Ms. Marianne L. Horinko
US Environmental Protection Agency
1200 Pennsylvania Ave., N. W.
Washington, DC 20460

Re: Revision of γ-Butyrolactone (96-48-0) Documents
Via Electronic Submission to: Oppt.ncic@epa.gov

Registered with EPA as:
BPPB Consortium, **Registration Number**

Dear Acting Administrator Horinko;

On behalf of the BPPB Consortium, Toxicology and Regulatory Affairs is hereby responding to the U.S. EPA's comments posted June 19, 2003 on the Chem-RTK HPV Challenge Web site for the Test Plan and Robust Summaries of γ-Butyrolactone (CASNO 96-48-0). The U.S. EPA's comments can be broadly grouped into two categories; testing related comments and comments pertaining to information in the Test Plan or Robust Summaries. The following are responses to the U.S. EPA's comments/questions based on these two groups:

Testing Related Issues

U.S. EPA Comment (1): The submitter needs to provide separate robust summaries for the evaluation of reproduction organs from the two NTP repeated-dose toxicity studies.

BPPB Response (1): Additional information regarding organs examined and individual animal pathology results were obtained courtesy of the NTP. A single robust summary was prepared and added in the "Fertility" section giving information on the evaluation of the reproduction organs from the two NTP repeated-dose toxicity studies in rats and mice.

U.S. EPA Comment (2): The available fish study is inadequate to satisfy the endpoint and the submitter needs to perform an acute fish toxicity study in accordance with OECD Guideline 203.

BPPB Response (2): An additional acute toxicity study of 96-hour duration has been located and added to the robust summaries as the critical study. This well-documented study demonstrates that there is no additional mortality from extending the duration of the study to 96 hours. We believe this additional study, which was located after preparation of the initial submission, fulfils the requirements of the U. S. EPA HPV program.

Test Plan and Robust Summaries

U.S. EPA Comment (3): For the algae study, the submitter needs to provide test substance purity and statistical methods used. The submitter also needs to clarify whether the reported 96-hour IC50/IC20 values were based upon measured or nominal concentration.

BPPB Response (3): The reported 96-hour IC_{50}/IC_{20} values were based upon nominal concentrations. All other relevant methodological details that were available in the study report were included in the robust summary. The purity is now indicated as unknown. The statistical procedure was not described in the report but a linear regression analysis of the log concentration versus inhibition yields an IC_{50} of 95.4 mg/L, suggesting that a similar but more conservative method was used for the calculation in the report.

The Test Plan and robust summaries have been revised to incorporate the changes noted above. The BPPB Consortium believes that these modifications and additions to the Robust Summaries and Test Plan fulfill all aspects of the U.S. EPA HPV program for γ-Butyrolactone (CASNO 96-48-0).

Sincerely,

Elmer Rauckman, PhD, DABT
Consulting Toxicologist

Attachments:

Testing Plan	96-48-0-Rev Test Plan.pdf
Robust Summaries	96-48-0-Rev RS.pdf